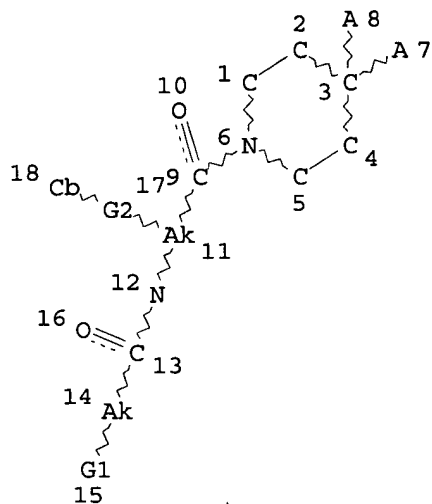


=> d l1
 L1 HAS NO ANSWERS
 L1 STR



VAR G1=N/HY
 REP G2=(0-3) CH
 NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RSPEC 1
 NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE

=> s l1 ful
 FULL SEARCH INITIATED 13:01:18 FILE 'REGISTRY'
 FULL SCREEN SEARCH COMPLETED - 201156 TO ITERATE

100.0% PROCESSED 201156 ITERATIONS
 SEARCH TIME: 00.00.10

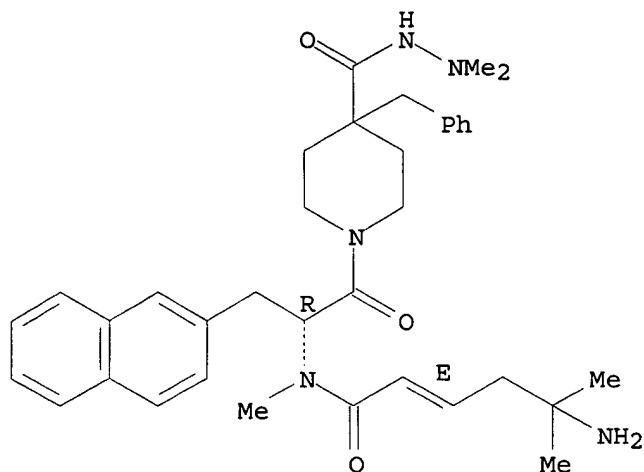
11 ANSWERS

L3 11 SEA SSS FUL L1

=> d scan

L3 11 ANSWERS REGISTRY COPYRIGHT 2003 ACS
 IN 4-Piperidinecarboxylic acid, 1-[(2R)-2-[[[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]methylamino]-3-(2-naphthalenyl)-1-oxopropyl]-4-(phenylmethyl)-, 2,2-dimethylhydrazide (9CI)
 MF C36 H47 N5 O3

Absolute stereochemistry.
 Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> fil caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

150.15

150.36

FILE 'CAPLUS' ENTERED AT 13:01:53 ON 21 APR 2003

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE COVERS 1907 - 21 Apr 2003 VOL 138 ISS 17

FILE LAST UPDATED: 20 Apr 2003 (20030420/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 2 L3

=> d bib abs hitstr 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS

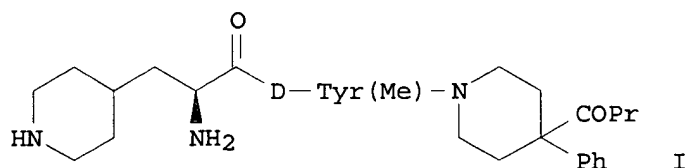
AN 2002:695975 CAPLUS

DN 137:232913

TI Preparation of peptides for pharmaceutical use as modulators of melanocortin receptors

IN Yu, Guixue; Macor, John; Herpin, Timothy; Lawrence, R. Michael; Morton, George C.; Ruel, Rejean; Poindexter, Graham S.; Ruediger, Edward H.; Thibault, Carl
 PA Bristol-Myers Squibb Company, USA
 SO PCT Int. Appl., 107 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|--|----------|-----------------|----------|
| PI | WO 2002070511 | A1 | 20020912 | WO 2002-US6479 | 20020302 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| PRAI | US 2001-273206P | P | 20010302 | | |
| | US 2001-273291P | P | 20010302 | | |
| OS | MARPAT 137:232913 | | | | |
| GI | | | | | |



AB Compds. W-(CR6R7)yCH(G)(CR4R5)xCO-X(R1)CHR2(CHR3)r(CH2)sCO-E [X = N or CH; R1, R3 = H or alkyl; R2 = H, aryl, cycloalkyl, heteroaryl, heterocyclyl, (un)substituted alkyl or alkenyl; R1 together with R2 or R3 or R2 together with R3 form mono- or bicyclic aryl, cycloalkyl, heteroaryl, or heterocyclyl; E = (un)substituted pyrrolidino, piperidino, hexahydro-1-azepinyl, 1-piperazinyl, cyclopentyl, cyclohexyl, cycloheptyl, amino, (cyclo)alkylamino; R4-R6 = H, (un)substituted alkyl, amino, alkylamino, hydroxy, alkoxy, aryl, cycloalkyl, heteroaryl, or heterocyclyl; or CR4R5 or C6R7 is a spirocycloalkyl ring; r, s = 0 or 1; x = 0-4; y = 0-2; G = alkenyl, arylalkenyl, hydroxy, heteroaryl, cyano, functionalized alkyl or alkenyl, etc.; W = amino, alkylamino, hydroxy, alkoxy, carbamoyl, amidino, cycloalkyl, heteroaryl, heterocyclyl, etc.] were prepd. as modulators of melanocortin receptors, particularly MC-1R and MC-4R. Thus, peptide I was prepd. by a soln.-phase peptide coupling/deprotection scheme.

IT 457903-95-6P 457904-39-1P

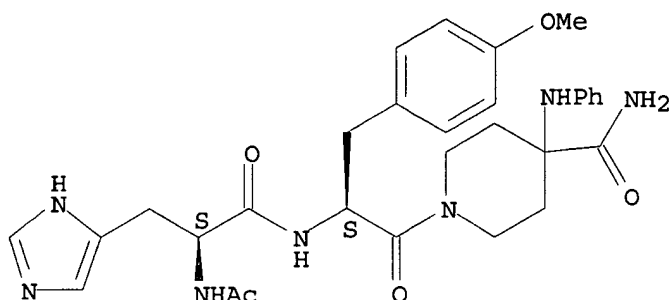
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptides for pharmaceutical use as modulators of melanocortin receptors)

RN 457903-95-6 CAPLUS

CN 4-Piperidinecarboxamide, 1-[(2S)-2-[[[(2S)-2-(acetylamino)-3-(1H-imidazol-4-yl)-1-oxopropyl]amino]-3-(4-methoxyphenyl)-1-oxopropyl]-4-(phenylamino)-(9CI) (CA INDEX NAME)

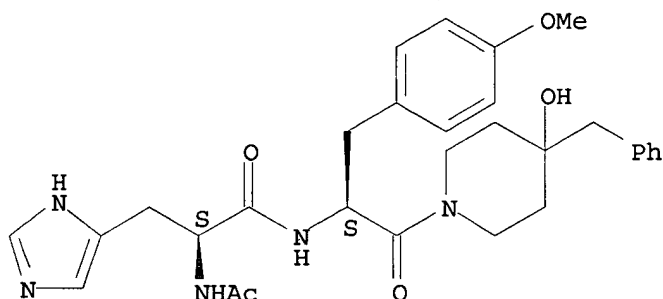
Absolute stereochemistry.



RN 457904-39-1 CAPLUS

CN 1H-Imidazole-4-propanamide, .alpha.-(acetylamino)-N-[(1S)-2-[4-hydroxy-4-(phenylmethyl)-1-piperidiny]-1-[(4-methoxyphenyl)methyl]-2-oxoethyl]-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS

AN 1999:736657 CAPLUS

DN 131:336948

TI Preparation of piperidine derivatives with growth hormone releasing properties

IN Hansen, Thomas Kruse; Ankersen, Michael

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 87 pp.

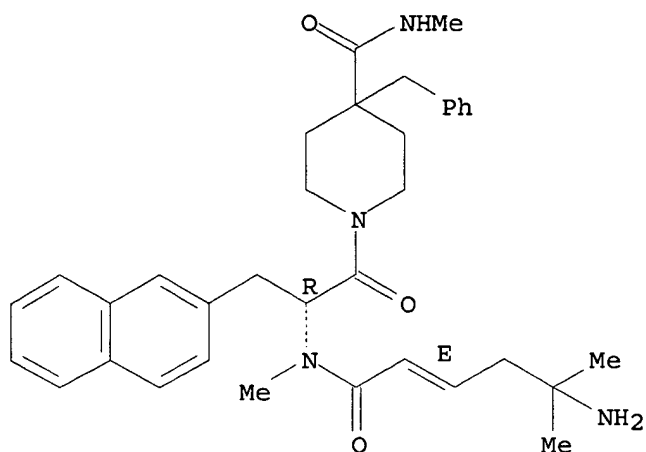
CODEN: PIXXD2

DT Patent

LA English

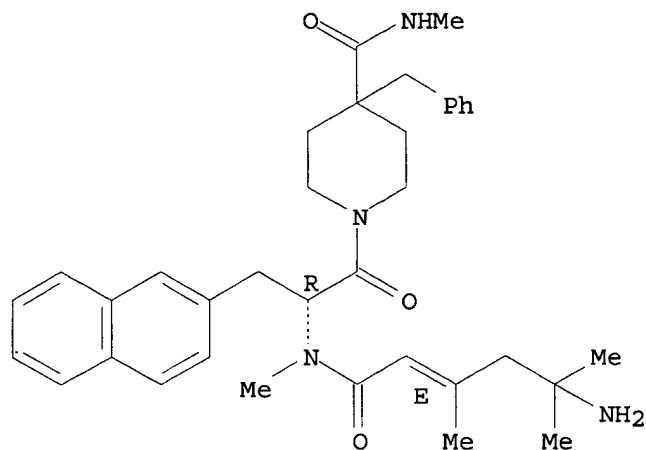
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|------------|--|----------|-----------------|----------|
| PI | WO 9958501 | A1 | 19991118 | WO 1999-DK260 | 19990510 |
| | W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| | US 6303620 | B1 | 20011016 | US 1999-306151 | 19990506 |



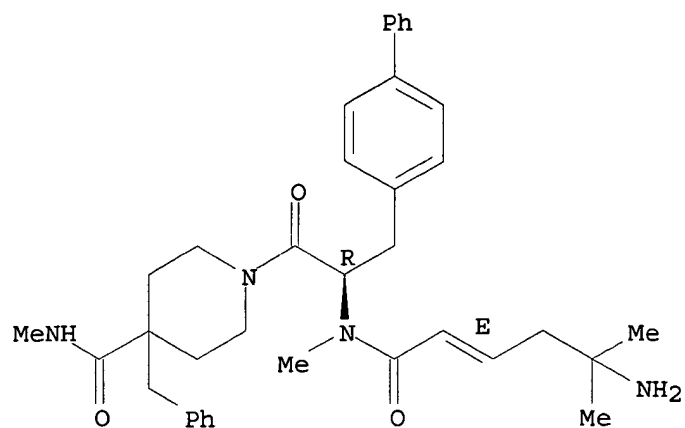
RN 249920-95-4 CAPLUS
 CN 4-Piperidinecarboxamide, 1-[(2R)-2-[[[(2E)-5-amino-3,5-dimethyl-1-oxo-2-hexenyl]methylamino]-3-(2-naphthalenyl)-1-oxopropyl]-N-methyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



RN 249920-96-5 CAPLUS
 CN 4-Piperidinecarboxamide, 1-[(2R)-2-[[[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]methylamino]-3-[1,1'-biphenyl]-4-yl-1-oxopropyl]-N-methyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

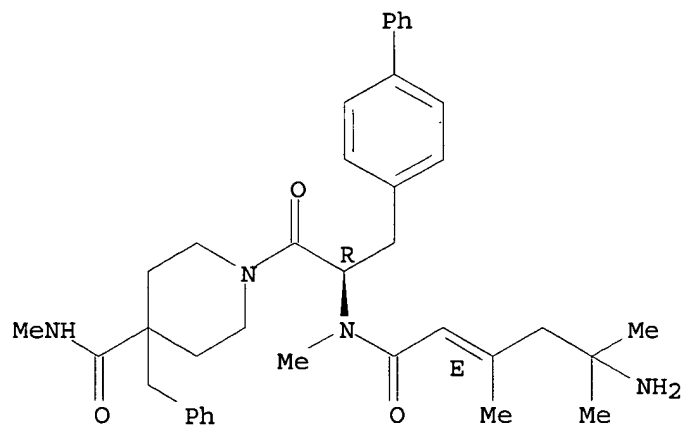
Absolute stereochemistry.
 Double bond geometry as shown.



RN 249920-97-6 CAPLUS

CN 4-Piperidinecarboxamide, 1-[(2R)-2-[[[(2E)-5-amino-3,5-dimethyl-1-oxo-2-hexenyl]methylamino]-3-[1,1'-biphenyl]-4-yl]-1-oxopropyl]-N-methyl-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

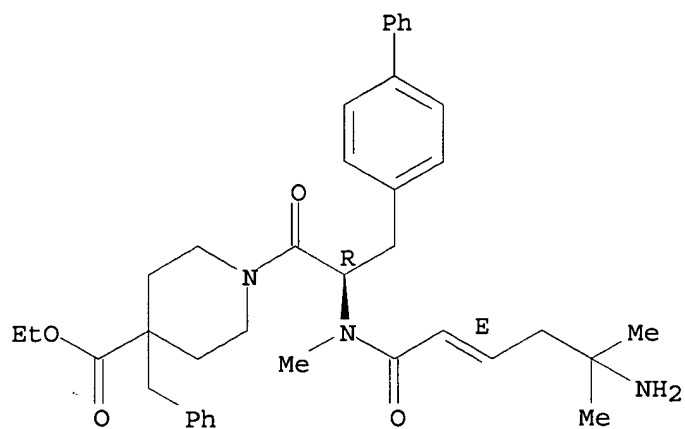
Absolute stereochemistry.
Double bond geometry as shown.



RN 249921-02-6 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[(2R)-2-[[[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]methylamino]-3-[1,1'-biphenyl]-4-yl]-1-oxopropyl]-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)

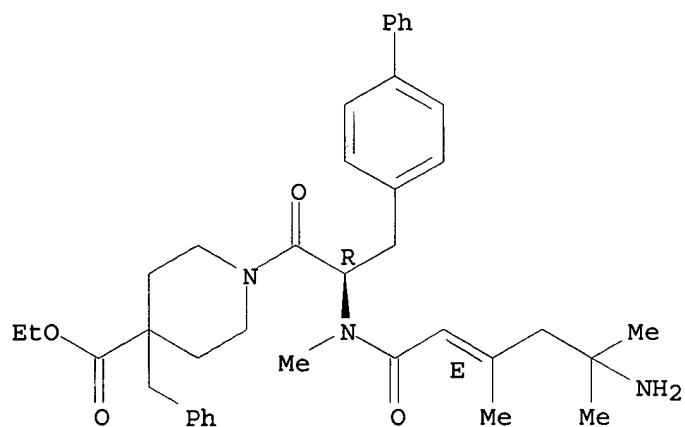
Absolute stereochemistry.
Double bond geometry as shown.



RN 249921-03-7 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[(2R)-2-[[[(2E)-5-amino-3,5-dimethyl-1-oxo-2-hexenyl]methylamino]-3-[1,1'-biphenyl]-4-yl-1-oxopropyl]-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)

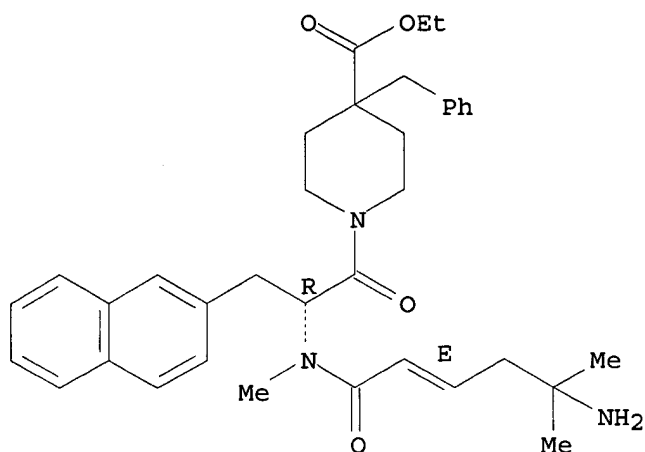
Absolute stereochemistry.
Double bond geometry as shown.



RN 249921-04-8 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[(2R)-2-[[[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]methylamino]-3-(2-naphthalenyl)-1-oxopropyl]-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)

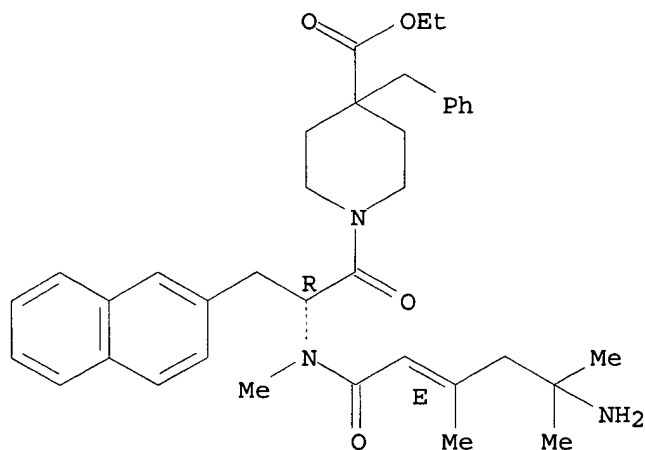
Absolute stereochemistry.
Double bond geometry as shown.



RN 249921-05-9 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[(2R)-2-[[[(2E)-5-amino-3,5-dimethyl-1-oxo-2-hexenyl]methylamino]-3-(2-naphthalenyl)-1-oxopropyl]-4-(phenylmethyl)-, ethyl ester (9CI) (CA INDEX NAME)

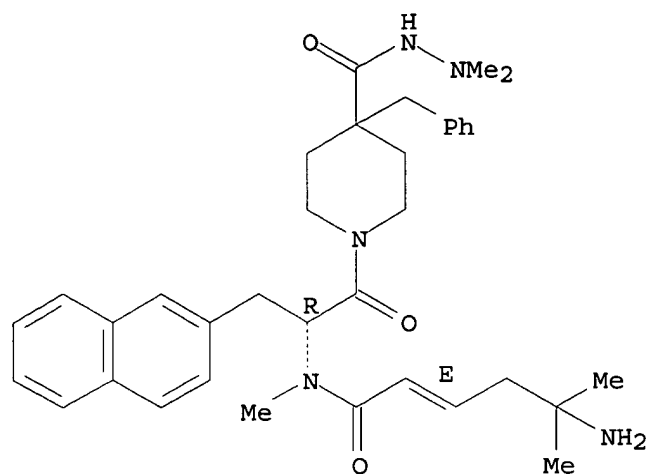
Absolute stereochemistry.
Double bond geometry as shown.



RN 249921-09-3 CAPLUS

CN 4-Piperidinecarboxylic acid, 1-[(2R)-2-[[[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]methylamino]-3-(2-naphthalenyl)-1-oxopropyl]-4-(phenylmethyl)-, 2,2-dimethylhydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 8

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s melanocortin?
 L5 1281 MELANOCORTIN?
 => s 15(1)piperidin?
 80708 PIPERIDIN?
 L6 24 L5(L) PIPERIDIN?
 => s 16 and triazo?
 36601 TRIAZO?
 L7 5 L6 AND TRIAZO?
 => d bib abs 1-5

L7 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS
 AN 2002:822284 CAPLUS
 DN 138:131392
 TI Activation of melanocortin MC4 receptors increases erectile activity in rats ex copula
 AU Martin, William J.; McGowan, Erin; Cashen, Doreen E.; Gantert, Liza T.; Drisko, Jennifer E.; Hom, Gary J.; Nargund, Ravi; Sebhat, Iyassu; Howard, Andrew D.; Van der Ploeg, Lex H. T.; MacIntyre, D. Euan
 CS Department of Pharmacology, Merck Research Laboratories, Rahway, NJ, 07065, USA
 SO European Journal of Pharmacology (2002), 454(1), 71-79
 CODEN: EJPHAZ; ISSN: 0014-2999
 PB Elsevier Science B.V.
 DT Journal
 LA English
 AB **Melanocortin** peptide agonists, .alpha.-MSH and melanotan-II, stimulate erectile activity in a variety of species, including man. Since neither peptide discriminates amongst **melanocortin** receptors, it is not clear which subtype mediates these pro-erectile effects. Here, the authors present data that **melanocortin**-induced erectogenesis is mediated by **melanocortin** MC4 receptors. Systemic administration of a **melanocortin** MC4 receptor agonist (N-[(3R)-1,2,3,4-tetrahydroisoquinolinium-3-ylcarbonyl]-(1R)-1-(4-chlorobenzyl)-2-[4-cyclohexyl-4-(1H-1,2,4-triazol-1-yl methyl)**piperidin**-1-yl]-2-oxoethylamine; THIQ) with high selectivity over other **melanocortin** receptors enhanced intracavernosal pressure and stimulated erectile activity in rats ex copula. THIQ dose-dependently (1-5 mg/kg, i.v.) increased the total no. of erections, to an extent comparable or greater than that produced by apomorphine (0.025 mg/kg, s.c.). Central administration of THIQ (20 .mu.g, intracerebroventricular (i.c.v.)) increased the no. of reflexive penile erections; whereas administration of both a nonselective endogenous **melanocortin** MC4 receptor antagonist (agouti-related protein (AgRP), 5.5 .mu.g, i.c.v.) and a **melanocortin** MC4 receptor preferring antagonist (MPB10, 1 mg/kg, i.v.) blocked THIQ-induced erectogenesis. These pro-erectile effects were also attenuated by systemic or central administration of an oxytocin antagonist (L-368899, 1 mg/kg, i.v.). Thus, **melanocortin** MC4 receptor activation is sufficient for erectogenesis and these effects may involve oxytocinergic pathways.
 RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS
 AN 2002:699493 CAPLUS
 DN 137:362928
 TI Design and pharmacology of N-[(3R)-1,2,3,4-tetrahydroisoquinolinium-3-ylcarbonyl]-(1R)-1-(4-chlorobenzyl)-2-[4-cyclohexyl-4-(1H-1,2,4-triazol-1-ylmethyl)**piperidin**-1-yl]-2-oxoethylamine (1), a potent, selective, **melanocortin** subtype-4 receptor agonist

AU Sebhat, Iyassu K.; Martin, William J.; Ye, Zhixiong; Barakat, Khaled; Mosley, Ralph T.; Johnston, David B. R.; Bakshi, Raman; Palucki, Brenda; Weinberg, David H.; MacNeil, Tanya; Kalyani, Rubana N.; Tang, Rui; Stearns, Ralph A.; Miller, Randy R.; Tamvakopoulos, Constantin; Strack, Alison M.; McGowan, Erin; Cashen, Doreen E.; Drisko, Jennifer E.; Hom, Gary J.; Howard, Andrew D.; MacIntyre, D. Euan; van der Ploeg, Lex H. T.; Patchett, Arthur A.; Nargund, Ravi P.

CS Departments of Chemistry, Pharmacology, Obesity Research, and Drug Metabolism, Merck Co. Inc., Rahway, NJ, 07065-0900, USA

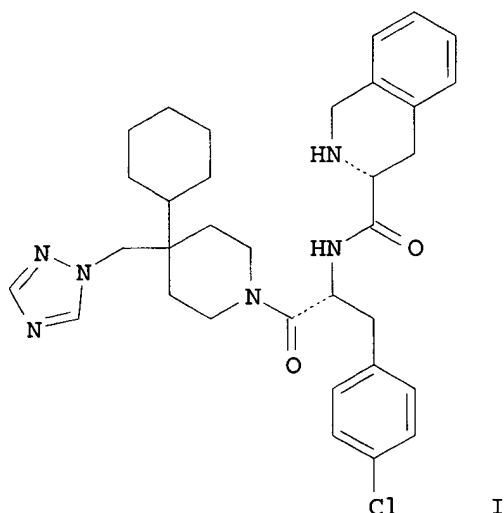
SO Journal of Medicinal Chemistry (2002), 45(21), 4589-4593
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

GI



AB Synthetic and natural peptides that act as nonselective melanocortin receptor agonists have been found to be anorexigenic and to stimulate erectile activity. We report the design and development of (I), a potent, selective (1184-fold vs. MC3R, 350-fold vs. MC5R), small-mol. agonist of the MC4 receptor. Pharmacol. testing confirms the food intake lowering effects of MC4R agonism and suggests another role for the receptor in the stimulation of erectile activity.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS

AN 2002:675992 CAPLUS

DN 137:216873

TI Acylated **piperidine** derivatives, specifically
1-(pyrrolidinylcarbonyl)**piperidines**, 1-(
piperidinylcarbonyl)**piperidines**, and analogs, as
melanocortin-4 receptor agonists, and their pharmaceutical
compositions and therapeutic uses

IN Goulet, Mark T.; Nargund, Ravi P.; Sebhat, Iyassu K.; Ujjainwalla, Feroze; Walsh, Thomas F.; Warner, Daniel; Young, Jonathan R.; Bakshi, Raman K.

PA Merck & Co., Inc., USA; Ye, Zhixiong

SO PCT Int. Appl., 138 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|--|----------|-----------------|----------|
| PI | WO 2002068387 | A2 | 20020906 | WO 2002-US5623 | 20020225 |
| | WO 2002068387 | A3 | 20030220 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| PRAI | US 2001-272258P | P | 20010228 | | |
| | US 2001-300572P | P | 20010622 | | |
| OS | MARPAT 137:216873 | | | | |
| GI | | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Certain novel 4-substituted N-acylated **piperidine** derivs., specifically I, are agonists of the human **melanocortin** receptor(s) and, in particular, are selective agonists of the human **melanocortin-4** receptor (MC-4R) [wherein: p = 1 or 2; q = 0, 1, or 2; n = 0, 1, or 2; R1 = H, amidino, alkyliminoyl, (un)substituted alkyl, (CH2)n-G1 [G1 = (un)substituted cycloalkyl, Ph, naphthyl, or heteroaryl]; R2 = (un)substituted Ph, naphthyl, or heteroaryl; X = alkyl, (CH2)n-G2 [G2 = (un)substituted cycloalkyl, Ph, naphthyl, heteroaryl, heterocyclyl, cyano, CONH2, CO2H, OH, NH2, and various derivs.]; Y = (un)substituted alkyl, alkenyl, (CH2)n-G3 [G3 = (un)substituted cycloalkyl, Ph, naphthyl, heteroaryl, or heterocyclyl]; including pharmaceutically acceptable salts]. They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, sexual dysfunction, including erectile dysfunction and female sexual dysfunction. Approx. 200 invention compds. I and approx. 80 intermediates were prepd. For instance, amidation of (.+-.)-trans-1-(tert-butoxycarbonyl)-3-(4-fluorophenyl)**piperidine**-4-carboxylic acid with 4-cyclohexyl-4-[(4,4-dimethyl-2-oxo-1,3-oxazolidin-3-yl)methyl]**piperidine** HCl, followed by N-deprotection with removal of BOC using HCl, and reductive N-methylation using paraformaldehyde and NaBH3CN, gave title compd. (.+-.)-trans-II, isolated as the trifluoroacetate salt. Representative compds. I bound to cloned human MC-4R in vitro with IC50 values generally below 2 .mu.M, and also acted as agonists toward cloned human MCR in a functional assay with EC50 values less than 1 .mu.M.

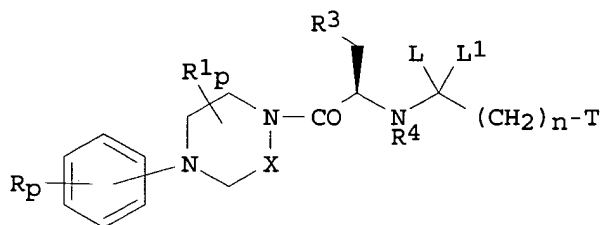
L7 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
AN 2002:575066 CAPLUS
DN 137:140777

TI Preparation of piperazinyl and hexahydro-1,4-diazepinyl amino acid derivatives as melanocortin receptor agonists
IN Biggers, Christopher Kelly; Briner, Karin; Doecke, Christopher William; Fisher, Matthew Joseph; Hertel, Larry Wayne; Mancoso, Vincent; Martinelli, Michael John; Mayer, John Philip; Ornstein, Paul Leslie; Richardson, Timothy Ivo; Shah, Jikesh Arvind; Shi, Qing; Wu, Zhipei; Xie, Chaoyu
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 356 pp.

CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-------------------|--|----------|-----------------|----------|
| PI | WO 2002059108 | A1 | 20020801 | WO 2002-US517 | 20020123 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| PRAI | US 2001-263471P | P | 20010123 | | |
| OS | MARPAT 137:140777 | | | | |
| GI | | | | | |



I

AB The invention relates to melanocortin receptor (MC-R) agonists I [X = CH₂ or CH₂CH₂; LL₁ = H₂ or oxo; T = isoquinolinyl or tetrahydro deriv., isoindolinyl, or piperazinyl; n = 0-8; R = H, OH, CN, NO₂, halo, alkyl, acyl, etc.; R₁ = H, alkyl, alkylcarbamoyl, (D)phenyl, (D)cycloalkyl, or oxo (unless amide is formed); p = 0-5; R₃ = (un)substituted aryl or thienyl; R₄ = H, alkyl, acyl, cycloalkyl, or alkoxyalkyl], or their pharmaceutically-acceptable salts or stereoisomers, which are useful in the treatment of obesity, diabetes, and male and/or female sexual dysfunction. Comps. I comprise three domains, i.e., a piperazinyl or hexahydro-1,4-diazepinyl fragment, an amino acid, and a radical CLL₁(CH₂)_n-T. Thus, 1-(D-Tic-4-Cl-D-Phe)-4-[2-(methanesulfonylamino)phenyl]piperazine (Tic = 1,2,3,4-tetrahydroisoquinoline-3-carbonyl; claimed compd.) was prepd. via acylation of the piperazine moiety.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS

AN 2000:880962 CAPLUS

DN 134:42445

TI Preparation of **piperidine** amino acid derivatives as
melanocortin-4 receptor agonists

IN Bakshi, Raman K.; Barakat, Khaled J.; Nargund, Ravi P.; Palucki, Brenda L.; Patchett, Arthur A.; Sebhat, Iyassu; Ye, Zhixiong; Van, Der Ploeg Leonardus H. T.

PA Merck & Co., Inc., USA; Van Der Ploeg, Leonardus H. T.

SO PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| PI | WO 2000074679 | A1 | 20001214 | WO 2000-US14930 | 20000531 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1187614 | A1 | 20020320 | EP 2000-937961 | 20000531 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | JP 2003505435 | T2 | 20030212 | JP 2001-512328 | 20000531 |
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| OS | MARPAT 134:42445 | | | | |
| GI | | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB **Piperidine** derivs. I [R2C2 = aryl, 5- or 6-membered heteroaryl or heterocyclyl, 5- to 7-membered carbocyclyl, which may be substituted; L = (CRb2)m, where Rb = H, alkyl, (CH2)n-cycloalkyl or -aryl; m = 0-2, n = 0-3; X, Y = (CH2)0-2; Ra = H, alkyl, (CH2)n-cycloalkyl, -aryl, -heteroaryl, -O(CH2)n-aryl, which may be substituted; Re = H, alkyl, (CH2)n-aryl, -cycloalkyl, -heteroaryl, which may be substituted, acyl, sulfonyl, etc.; R1 = H, alkyl, (CH2)n-cycloalkyl, -aryl, -heteroaryl, -heterocyclyl; R2 = any group given for R1, CN, (CH2)n-carboxamido, -carboxy, -acylamino, sulfonylamino, -amino, etc.] were prepd. as agonists of the human **melanocortin** receptors, in particular, the human **melanocortin-4** receptor (MC-4R). They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, sexual dysfunction, including erectile dysfunction and female sexual dysfunction. Thus, II trifluoroacetate, prepd. by coupling of Et 1-(D-4-chlorophenylalanyl)-4-cyclohexyl-4-[(1,2,4-triazol-1-yl)methyl]**piperidine** trifluoroacetate (prepn. given) with N-tert-butoxycarbonyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Boc-D-Tic), was > 2,200-fold, > 10,000-fold, and > 580-fold selective for the human MC-4R over human MC-1R, MC-2R, and MC-3R, resp.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
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